

REMARKS

Claims 1, 4, 5, 8 to 14, 16 to 18 and 20 and 21 are pending in the application; claims 2, 3, 6, 7 and 15 were previously canceled; claim 19 is presently canceled; and claims 20 and 21 are newly entered. The Office Action has indicated that claims 10 to 13 are free of the prior art. Claims 20 and 21 contain limitations previously found in dependent claim 8.

Claim 1 has been further amended to more clearly set forth the steps that comprise the method claimed, in acceptable format and also distinguishing over the prior art. The conditions for the steps have now been integrated into the steps themselves. Antecedent basis for “substrate” is found in line 2 of claim 1, and antecedent bases for “solution” in line 21 of claim 1 is found in line 5 thereof. The limitation “electrochemical boundary layer” has been deleted. Clarifying amendments have been made to all claims (except claim 13) to obviate the rejections thereof based on Section 112, second paragraph. Regarding the amendment to claims 16 and 17, the skilled artisan would clearly understand that the crystalline structure of the layer of S-layer proteins would provide discrete bonding sites whereat the functional molecules would bond, and thus it is not unclear. **All amendments to the claims are directed to resolving the rejections thereof under Section 112.**

Regarding the rejection of claim 1 (and claim 14 as well, it is believed) regarding combining functional molecules to S-layer proteins, such bonding or combining is disclosed in Example 4 of the Specification as originally filed, wherein birch pollen allergen Bet v 1 is merged on the C-terminal end of an S-layer protein, using two glycine radicals as linkers. Further, such a process is well known in the art: for example, 1) in Sleytr *et al* (item 7), Section VII: “S-layers as Matrices For the Immobilization of Functional Molecules” (pp. 205-207); 2) in Küpçü *et al* (item 14), overall, and in particular the first paragraph of the discussion on page 283 and Figure 3; and 3) in Sleytr *et al* (item 15), fifth paragraph on page 263 “Foreign molecules are either directly linked to . . .”.

Claims 1, 4, 5, 8, 9, 14 and 16 to 19 stand rejected under 35 USC §103(a) as being unpatentable over claims 1 to 5 of Sleytr *et al* (U.S. Patent No. 6,296,700 B1) in view of Pum *et al* (Item No. 12 on Form 1449) and Pum *et al* (Item No. 9 on Form 1449), and if necessary in further view of Sleytr *et al* (Item No. 11 on Form 1449) or Küpcü *et al* (Item No. 14 on Form 1449) or Sleytr *et al* (Item No. 15 on Form 1449).

Claims 1 to 9 and 14 to 17 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Sleytr *et al* (U.S. Patent No. 6,296,700 B1) in view of Pum *et al* (Item No. 12 on Form 1449) and Pum *et al* (Item No. 9 on Form 1449), and if necessary in further view of Sleytr *et al* (Item No. 11 on Form 1449) or Küpcü *et al* (Item No. 14 on Form 1449) or Sleytr *et al* (Item No. 15 on Form 1449).

The invention as set forth in amended claim 1 is based on the principal concept of controlling the modifying process of the bonding of the S-layer molecules after their adsorption to the substrate surface in an electrochemical way. This electrochemical control is not obtained simply by general chemical measures such as variation of a pH value or of a concentration of a substance; rather, the invention achieves such electrochemical control by a reference electrode to control the difference of potential at the S-layer protein layer.

Applicants believe that claim 1, and in particular the distinct two steps of (i) depositing a layer of S-layer proteins, and (ii) forming a two-dimensional crystalline structure in that deposited layer of S-proteins, as well as (iii) the use of a reference electrode to vary the electrochemical potential, delimits the invention against prior art. Such electrochemical potential is known in electrochemistry but is not disclosed in the cited prior art references with respect to its use during depositing and two-dimensional crystallization of an S-layer protein layer. Moreover, a person of routine skill in the art will not find indications in the prior art to control the chemical conditions of the solution by electrochemical methods using an electrode arrangement. Rather, the prior art offers to the person

skilled in the art various methods of chemical (**only**) control presenting sufficient alternative ways to improve the process of deposition and crystallization of S-layers which are sufficient to lead him or her away from the invention.

Regarding the separate deposition and crystallization, prior art only refers to immobilization of S-layer proteins on a substrate, without conceptual of factual distinction of the stages of depositing S-layer proteins and forming a crystalline structure; sometimes the word “deposition” is known to be even indiscriminately used for the complete procedure.

Regarding controlling electrochemical conditions through electric potentials, the prior art employs only chemical (not electrochemical) procedures for depositing/immobilization of the S-layers; electrochemical procedures are only used afterwards: In particular, Pum *et al* (item 9) show deposition of an S-layer, immobilizing an enzyme onto that S-layer and then sputtering an electrode onto the enzyme layer (see Fig. 2 of Pum et al.). Neubauer *et al* (item 10) disclose electrochemical deposition of metallic material through the protein crystal pores *in situ* (lines 6 to 7 of page 2); this requires prior forming of a crystalline S-layer.

Most importantly, Pum *et al* (item 12) disclose that the S-layers “can be bound in dense monomolecular crystalline packing by either non-covalent forces (e.g., electrostatic interactions) or covalent bonds” (page 10, column 1, 4th from last line to line 2 of column 2). They demonstrate that this will produce a crystallized S-layer already when traditional chemical procedures are employed. Only after fixation of the S-layer, electrochemical methods are used, such as “sputtering a thin layer of gold onto the surface” as in the first complete paragraph of column 2 of page 10.

Therefore, the prior art teaches away from the feature of the claimed invention (i.e., performing the two steps of deposition and crystallization of the S-layer by controlling respective electrochemical conditions of the carrier surface through application of respective electrochemical

potentials to the substrate with respect to the reference electrode), in that the prior art suggest to use electrochemical procedures only after an S-layer is formed and fixed.

Applicants believe that amended claim 1 is novel and also is non-obvious over the prior art. By the same token, applicants also believe that the double patenting rejection is overcome.

CONCLUSION

In view of the foregoing, Applicants respectfully submit that claims 1, 4, 5, 8 to 14, 16 to 18 and 20 and 21 are in condition for allowance. Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims. If there are any other fees due in connection with the filing of this response, please do not hesitate to contact the undersigned.

Respectfully Submitted,

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